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Bronchoscopy during the COVID-19 pandemic: A Canadian Thoracic Society Position Statement update

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Introduction

Since the beginning of the COVID-19 pandemic there have been nearly 4 million reported cases and over 42,000 deaths attributable to COVID-19 among Canadians.¹ During this time, healthcare systems in Canada have had to adapt in order to care for patients with COVID-19 infection, while trying to maintain non-COVID related services, all while managing the risk of infection transmission to patients, the public and health care practitioners (HCPs).

The nature of the COVID-19 pandemic has changed dramatically since the first wave in Canada in early 2020, particularly due to the emergence of new dominant variant viral strains, and the adoption of policies to mitigate infection, including widespread vaccination. As we move towards the endemic phase of COVID-19, HCPs must continue to adopt the latest evidence in providing care to patients affected by COVID-19, while aiming to safely return to near-normal levels of care provision in other areas.

This update to the Bronchoscopy during the COVID-19 pandemic statement² aims to provide guidance to bronchoscopists and other HCPs performing or participating in bronchoscopy. These recommendations are informed by a limited body of evidence as well as position statements and guidelines from other international expert groups. These recommendations are subject to change as information regarding COVID-19 and its effects are further understood. We plan to update this guidance as new information becomes available. We recommend checking the Canadian Thoracic Society (CTS) website (<https://cts-sct.ca/covid-19/>) for updates.

Patient evaluation prior to bronchoscopy

Key statements

- Patients undergoing bronchoscopy should be systematically screened for symptoms and risk factors for active respiratory infection including COVID-19 48-72 hours prior to the procedure and upon arrival for the procedure.
- Non-urgent bronchoscopies should generally be delayed for patients with a positive symptom screen or test.
- Bronchoscopy providers should follow the most recent guidance regarding ending isolation and precautions for people with COVID-19 to determine when elective bronchoscopy may be safely performed in patients with COVID-19 infection.
- Pre-procedure COVID-19 viral testing for asymptomatic patients should be done at the discretion of individual healthcare facilities.
- Facilities requiring pre-procedure COVID-19 viral testing for asymptomatic individuals prior to bronchoscopy should aim to avoid procedure cancellations due to missed testing or test results. Regardless of pre-procedure protocols for symptom screening or testing, universal strategies to reduce transmission are recommended for all bronchoscopies as outlined elsewhere in this document. Systematic screening for symptoms of COVID-19 infection and risk factors for developing infection is recommended for all patients prior to bronchoscopy except where bronchoscopy is performed for diagnosis of COVID-19 or to investigate for complications or co-infections in a patient known to have COVID-19 infection. Although physical strategies to mitigate infection such as full personal protective equipment (PPE) and use of negative pressure spaces (as defined elsewhere in this document) help protect HCPs performing the procedure, delaying elective bronchoscopy

for patients with transmissible infection should be part of a broader strategy to prevent COVID-19 transmission within health care facilities.

Systematic screening for symptoms of COVID-19 and risk factors for developing infection should be performed 48–72 hours prior to the procedure. Patients should also be screened upon arrival. A standard questionnaire should be used as recommended in a previous position statement.² Differentiating COVID-19 infection from other respiratory conditions based on symptoms may be difficult, and viral testing is likely to be required in these situations. Patients who screen positive for symptoms or risk factors for active respiratory infection should have a nasopharyngeal (NP) swab for a reverse transcription-polymerase chain reaction (RT-PCR) viral testing prior to their bronchoscopy, provided that the procedure can be safely delayed. A detailed list of indications for bronchoscopy that are considered emergent, urgent and elective are shown in Table 1.

The United States Centers for Disease Control and Prevention (CDC) provides updated guidance on ending isolation and precautions for persons with COVID-19.³ The recommended duration of isolation depends on the severity of illness, and whether the patient is immunocompromised. Repeat testing and consultation with infectious disease experts may be required in some cases. In general, non-emergent bronchoscopy may proceed once a patient with COVID-19 is no longer considered infectious (i.e., required to isolate or wear a mask) based on the CDC guidelines. For example, an immunocompetent person who is mildly or moderately ill from COVID-19 should wait at least 10 days from symptom onset, and 24 hours since last being febrile before undergoing elective or non-urgent bronchoscopy. Bronchoscopy providers should regularly review this guidance and ensure that their programs are adhering to the most recent recommendations.

The value of pre-procedure COVID-19 viral testing for asymptomatic patients prior to bronchoscopy is uncertain. The rationale for routine testing is that the average period of infectiousness for COVID-19 begins 2–3 days prior symptoms, and peaks just prior to symptom onset.³ Hence, screening for symptoms alone is not completely protective. Separate reports of routine viral testing prior to surgical procedures during the first wave of the pandemic showed a range of positivity rates from 0.13% to 8% from different geographic regions.^{4–8} This wide range reflects regional differences in transmission rates during the first wave of the pandemic. A high correlation between negative NP swab testing, and negative lower respiratory tract sampling in asymptomatic patients undergoing bronchoscopy has been shown.⁹ Therefore, HCPs can have a high degree of confidence that patients are not infectious through a combination of negative symptom screening and a negative NP test in low-risk patients.

For patients undergoing surgery, a large multinational cohort study by the COVIDSurg Collaborative has shown that perioperative COVID-19 infection contributes to an increased risk for adverse outcomes.¹⁰ Additionally, a negative test for COVID-19 prior to surgery was associated with a reduced risk of post-operative pulmonary

complications.¹¹ A 7-week delay for elective surgeries has been suggested in order to reduce the risk to baseline.¹² The authors are unaware of any data to suggest that patients with asymptomatic COVID-19 infection are at increased risk of adverse outcomes related to elective bronchoscopy. Therefore, the value of COVID-19 testing prior to bronchoscopy is primarily in the anticipated reduction of infection transmission, rather than benefit to the individual patient.

The CDC recommends pre-procedural COVID-19 viral testing at the discretion of the facility and encourages providers to consider environmental factors, background rate of transmission and recency of vaccination status when making this decision.¹³ The authors agree with this recommendation. For example, testing is more likely to be of value in facilities with limited access to negative pressure spaces, or where recovery rooms are shared. Ideally, programs should also have access to current data on infection rates within their regions. Routine pre-procedure testing is expected to be more beneficial during phases of moderate loco-regional transmission (i.e., >25 infections per 100,000 persons). The impact of patient vaccination status on risk to HCPs during aerosol-generating medical procedures (AGMP) is not well characterized. While COVID-19 vaccination has consistently been shown to reduce the risk of severe outcomes, vaccines are not completely effective in preventing infection, especially for current and emerging variants.¹⁴ At present, it is not clear that patient vaccination should be a factor in pre-procedural testing.

The CDC has advised that patients who have recovered from COVID-19 may continue to test positive by NP swab due to persistent levels of detectable SARS-CoV-2 ribonucleic acid (RNA) in the upper respiratory tract for up to 3 months. However, these patients are generally not considered infectious.³ Therefore, a positive test result should always be interpreted in context of recent infection.

Unfortunately, access to NP swab PCR testing is not consistent across Canada. Patients may have difficulty accessing testing for many reasons. The authors believe that programs requiring routine viral testing for asymptomatic patients have a responsibility to ensure that patient care is not compromised by missed tests or test results, especially for disadvantaged patients. Programs should develop a back-up protocol such as performing rapid diagnostic RT-PCR testing on the day of the procedure or proceeding with the procedure as the last case of the day when necessary.

Prevention of infection transmission

Key statements

- COVID-19 may be spread through aerosolized droplets.
- The risk of COVID-19 transmission to HCPs from bronchoscopy is low provided that full PPE including an N-95 or equivalent respirator, gown, gloves and face shield is used.
- Bronchoscopy should be performed in a negative pressure space.

Table 1. Indications for bronchoscopy.

Emergent bronchoscopy	Urgent bronchoscopy	Elective bronchoscopy
<ul style="list-style-type: none"> massive hemoptysis severely symptomatic central airway obstruction^a 	<ul style="list-style-type: none"> moderately symptomatic central airway obstruction foreign body removal^a suspicion of lung cancer (lung mass and/or mediastinal or hilar adenopathies) diagnosis of pulmonary tuberculosis (TB) (where induced sputum is unavailable) suspicion of infection in immunocompromised patients Diagnosis of infection in a non-sputum producing patient^b investigation for mild to moderate hemoptysis evaluating progressive interstitial lung disease 	<ul style="list-style-type: none"> stable interstitial lung disease chronic cough suspicion of sarcoidosis where there is no indication to initiate therapy mildly symptomatic central airway obstruction therapeutic bronchoscopy for airway disease lung volume reduction bronchial thermoplasty evaluation of tracheobronchomalacia suspicion of non-TB mycobacterial infection Surveillance in patients with underlying lung disease

^aIn the pediatric population emergency bronchoscopy is routine for congenital airway malformations and foreign body removal.

^bIn pediatrics, bronchoscopy is commonly performed to diagnose infection in a non-sputum producing patient or as surveillance in patients with certain underlying lung diseases.

- Following bronchoscopy, patients should be recovered in individual spaces with adequate negative pressure ventilation.
- All HCPs involved in bronchoscopy should be fully vaccinated against COVID-19 in accordance with provincial guidelines.
- Disposable, single-use bronchoscopes should be considered for use when available in patients with known or suspected COVID-19 infection, particularly for simple bronchoscopic procedures in critical care settings. Since the publication of the last CTS position statement on bronchoscopy during COVID-19, the Public Health Agency of Canada and the CDC have advised that COVID-19 can be spread via aerosolized droplets.^{15,16} Prior to this, there was generalized early adoption of airborne precautions with full PPE and use of negative pressure spaces for bronchoscopy and other AGMPs. This was based on experience with previous respiratory viral outbreaks including severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and influenza. It is probable that this cautious approach prevented numerous outbreaks among HCPs from AGMP.

While COVID-19 variants of concern have demonstrated increased transmissibility, the available evidence suggests that the risk of transmission attributable to bronchoscopy in COVID-19 infected patients appears to be low.¹⁷⁻¹⁹ This data comes from a series of single-center retrospective reports, primarily in intubated patients. A review of these studies reveals limited rigor in the surveillance of

participating HCPs for developing infection, and that the primary focus was generally on the risk to bronchoscopists.²⁰⁻²⁶ Full protective PPE were used in all studies, and negative pressure spaces in some but not all. Negative pressure spaces are defined as 6-12 air exchanges per hour with a pressure differential between outside and inside the room of ≥ 2.5 Pa.²⁷

Factors that contribute to the risk of transmission from AGMP have been reported. Shorter physical distance and elevated patient viral load increase airborne COVID-19 particles, while adequate room ventilation (with mobile high-efficiency particulate air [HEPA] filter or built-in negative pressure systems) decreases airborne COVID-19 detection.^{28,29} All patients should don a close-fitting medical grade mask upon completion of bronchoscopy if tolerated, especially where individual negative pressure spaces for recovery are unavailable. Patients with known or suspected COVID-19 infection should be recovered in the endoscopy room rather than a common recovery area in facilities without individual negative pressure recovery spaces. Procedures deemed high risk for infection transmission should also be completed at the end of the day when possible.

Since the last CTS position statement on bronchoscopy during COVID-19, vaccinations against COVID-19 have been approved for all persons in Canada over 6 months old. Multiple vaccines are approved for use in Canada, and bivalent vaccines targeting variants are being administered as of September, 2022.^{30,31} In May 2022, 85% of the total Canadian population had been vaccinated with at least one dose, while nearly 82% had completed their primary series.³² Vaccines have been shown to significantly reduce morbidity and mortality from COVID-19 infection.³³ While protection wanes after a complete primary vaccine series (i.e., “fully vaccinated”), additional booster doses have been shown to significantly increase protection against novel variants.³⁴ Given the overwhelming evidence of benefit, and the need to protect the healthcare work force, all HCPs involved in bronchoscopy should be up to date with their COVID-19 vaccinations in accordance with provincial guidelines.

Disposable single-use bronchoscopes have become increasingly popular during the COVID-19 pandemic, especially in critical care settings. Multiple studies have reported similar efficacy between disposable and reusable bronchoscopes. Moreover, a systematic review and cost-effectiveness analysis found that single-use flexible bronchoscopes are associated with reduced risk of non-COVID-19 bronchoscopy-associated infections while maintaining cost-effectiveness.^{18,35} Although there is no direct evidence comparing transmission risk for COVID-19 between re-usable and disposable bronchoscopes, disposable flexible bronchoscopes should be considered for use in simple diagnostic and therapeutic procedures (ie, removal of secretions) for patients with known or suspected COVID-19 when available, particularly in critical care settings. For advanced procedures, re-usable bronchoscopes are usually preferred. When disposable bronchoscopes are not available or deemed inappropriate for use, post-procedure disinfection of re-usable bronchoscopes should be conducted as per national guidelines to prevent infection transmission.

Role of bronchoscopy in diagnosing COVID-19

Key statements

- An NP swab for RT-PCR for SARS-CoV-2 is recommended as the first test for the diagnosis of COVID-19 infection.
- When NP swab RT-PCR testing is negative, yet clinical suspicion of COVID-19 infection remains, bronchoscopy with bronchoalveolar lavage (BAL) should be performed for diagnosis of COVID-19 where a positive result will affect management.
- Computed tomography (CT) chest can be used to predict the probability of COVID-19 infection and should be used to help determine if diagnostic bronchoscopy is needed in patients with suspected infection despite a negative NP test. Diagnosis of COVID-19 infection relies on detection of SARS-CoV-2 virus from the respiratory tract, and persons suspected of COVID-19 require urgent diagnosis to facilitate management. Upper-respiratory tract sampling, typically via NP swab for RT-PCR testing is the preferred initial diagnostic test for COVID-19 infection given its ease, safety, accessibility, and accuracy.³⁶ Although upper and lower respiratory tract specimens are generally felt to have high concordance, BAL samples have been shown to have a higher sensitivity for detecting SARS-CoV-2 by RT-PCR than upper respiratory tract sampling. In an early study of hospitalized patients during the first wave of COVID-19 in China, Wang et al. evaluated body fluid specimens taken non-systematically for clinical purposes from infected inpatients. They noted a high positivity rate in BAL fluid samples relative to other sampled sites including NP swabs.³⁷ In several subsequent retrospective studies of critically ill patients, the reported diagnostic yield for BAL sampling in patients with suspected COVID-19 infection and negative RT-PCR testing by NP swab ranged from 12 to 51%.^{38–44} The time between negative NP swab and lower respiratory tract sampling was not consistently reported across studies. It is postulated that the quantity of virus in the upper and lower respiratory tracts varies depending on illness severity and time course, which is responsible for the perceived variation in test accuracy.

Inconsistent CT chest utilization as part of diagnostic decision-making may also contribute to variation in test results.⁴⁰ Four studies from the aforementioned series included descriptions of radiographic chest imaging in patients with suspected COVID-19 undergoing bronchoscopy.^{39,40,42,44} Four studies reported CT findings using the CO-RADS classification of CT findings.^{39,40,44,45} Among these studies there is good correlation between CT imaging consistent with COVID-19 infection, and positive BAL test after negative NP testing. In addition, in one study, Barberi et al. found that 5 out of 54 patients with a negative NP swab and CT findings felt to be inconsistent with COVID-19 still had a positive result from BAL.³⁹ This suggests that CT should not be used to rule out COVID-19 in patients where there is ongoing clinical suspicion. In general, bronchoscopy and BAL appears to be useful in confirming COVID-19

diagnosis in patients with consistent CT imaging (CO-RADS 4–5), and either establishing the diagnosis of COVID-19 or detecting an alternative cause in patients with indeterminate CT findings (CO-RADS 3).

To date, there is no evidence that COVID-19 variants affect the accuracy of diagnostic testing.⁴⁶ Additionally, the authors are unaware of any prospective studies comparing upper and lower respiratory tract sampling in patients with severe underlying immunocompromise.

Bronchoscopy for patients with known COVID-19 infection

Key statements

- Bronchoscopy can be safely performed in most patients with COVID-19 infection.
- Patients with COVID-19 infection requiring noninvasive ventilation (NIV) may be at higher risk of severe desaturation during bronchoscopy.
- Bronchoscopy is useful for clearing secretions in critically ill patients with COVID-19.
- Bronchoscopy is recommended for the diagnosis of superimposed fungal infections in critically ill patients with COVID-19.
- Bronchoscopy can be useful in evaluating patients for noninfectious pulmonary complications following acute COVID-19 infection, including organizing pneumonia. Although the use of bronchoscopy decreased early in the COVID-19 pandemic due to safety concerns, more recent studies have shown that bronchoscopy can safely be performed in adult patients with known COVID-19 infection with minimal risk to HCPs with the caveat that adequate PPE and environmental precautions are used.^{47,48} Through a systematic review of bronchoscopy in COVID-19 patients, Saha et al. established that complications from bronchoscopy in mechanically ventilated patients were minor and infrequent.⁴⁷ The most common complication across studies was transient desaturation ($\text{SpO}_2 < 90\%$). There were no reports of pneumothorax, arrhythmia or death. Conversely, in a small number of patients requiring noninvasive ventilation, bronchoscopy was associated with an increased risk of severe hypoxemia requiring intubation. In the majority of adult patients with known COVID-19 infection, bronchoscopy should not be avoided due to perceived safety concerns where it is clinically indicated, provided that appropriate precautions and monitoring are adhered to.

Since the beginning of the pandemic, important infectious and noninfectious pulmonary sequelae of acute COVID-19 infection have been increasingly described. Some of the earliest studies of bronchoscopy in critically ill patients with COVID-19 reported the presence of thick mucoid secretions in intubated patients.^{23,25} Bronchoscopy in this setting appears to be useful for clearing secretions in order to improve atelectasis and maintain oxygenation.⁴⁷

Superimposed invasive fungal infections have been reported in patients with COVID-19.^{49–51} COVID-19

associated pulmonary aspergillosis (CAPA) has been reported in 4 to 35% of adult patients with COVID-19 requiring ICU admission.⁵² This range in reported incidence may be related to heterogeneity in the diagnostic definitions used, and the extent to which CAPA is investigated for. It is also postulated that a reluctance to perform bronchoscopy due to safety concerns may be another factor.⁵² In addition to severe COVID-19 infection, high-dose corticosteroid treatments and underlying chronic lung disease have been identified as risk factors for CAPA in this population.⁵³ The rate of CAPA is expected to increase with the use of immunosuppressive therapies for COVID-19.⁴⁹ The diagnosis of CAPA has consistently been linked to increased mortality.^{49,52,54–56}

Bronchoscopy for visualization of tracheobronchitis, and BAL for fungal culture and detection of galactomannan is the standard for the clinical diagnosis of CAPA.^{49,52,54} Both serum galactomannan and beta-D-glucan have poor sensitivity for diagnosis of CAPA.^{52,54,57} Additionally, imaging findings in the setting of severe COVID-19 infection are often nonspecific and overlapping, and cannot reliably predict invasive fungal disease.^{57,58} Non-BAL bronchial samples have been used to investigate for CAPA, but are felt to be less specific, and may result in misdiagnosis.⁵⁴

COVID-19 associated pulmonary mucormycosis (CAPM) during or after COVID-19 pneumonia has also been increasingly reported but appears to be less common than CAPA overall.⁵⁰ Poorly controlled diabetes mellitus and corticosteroid use appear to be important risk factors.^{50,59} Bronchoscopy with BAL with or without tissue sampling is recommended for early identification CAPM, as no diagnostic serological markers exist at present.⁶⁰

Following resolution of acute infection, a range of radiographic parenchymal lung abnormalities have been reported in adult patients.⁶¹ Han and colleagues found that abnormal radiographic changes were persistent at 6 months in 27–35% of patients.⁶² A separate systematic review found that 26% of patients had evidence of fibrotic lung disease that persisted up to 12 months after infection.⁶³ The authors are not aware of any similar case series describing the long term radiologic sequelae in pediatric patients.

The histologic characteristics of persistent radiographic findings have been characterized in detail using transbronchial cryobiopsy. Ravaglia et al. described three clusters of combined clinical, radiographic, and pathological findings: patients with probable underlying chronic fibrosis, those with acute/subacute changes including organizing pneumonia, and patients with vascular changes associated with minimal radiographic abnormalities felt to be akin to pulmonary capillary hemangiomatosis.⁶¹

The development of organizing pneumonia (OP) following COVID-19 has been of particular concern in patients with subacute respiratory symptoms. The rate of developing OP following acute respiratory distress syndrome in the setting of COVID-19 infection is reportedly as high as 12.5% in adults.⁶⁴ This is likely overestimated, since radiographic findings are often non-specific, and surgical biopsy is considered the gold standard for the diagnosis of OP.⁶⁵ Several recent reports describe patients receiving treatment based

on clinical and radiographic features only.^{64,66,67} Where patients cannot undergo surgical biopsy for suspected OP, bronchoscopy is commonly used to rule out other diseases with similar clinical and radiographic presentation, especially secondary bacterial or fungal infections.⁶⁸

Conclusion

The nature of the COVID-19 pandemic has changed dramatically since the first wave in Canada. The emergence of new dominant variant viral strains, the adoption of policies to mitigate infection, and the development of COVID-19 vaccinations and therapies have had major impacts on our collective approach to this novel infection. As we move towards the endemic phase of COVID-19, HCPs must continue to adopt the latest evidence in providing care to patients affected by COVID-19, while aiming to safely return to near-normal levels of care provision in other areas.

Disclosure statement

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